

## BOOKS FOR SALE.

The following books are for sale by the widow of a recently deceased physician. Address Mrs. H. G. Plymire, 1510 Fifth avenue, Oakland, Calif.:

Medicine, Hare, 3 vols., 1905; Diagnostic Methods, Webster, 1909; Genito-Urinary Diseases, Gaspers, 1909; 12th Edition Therapeutics, *Materia Medica*, Pharmacy, Potter, 1912; Pathology, Coplin, 1911; Surgery, Spencer & Gask, 1910; Surgery, Binnie, 1911; 2 vols. Urology, Guiteras, 1912; Skin, Jackson, 1899; Surgical Therapeutics, Lanphear, 1907; 10 vols. Practice of Medicine, Series; Othology, Bacon; Hernia, Murry; 2 vols. Medicine, Strumpell, 1911; Anus, Rectum, Pelvic Colon, Tuttle, 1907; Preparatory and After Treatment in Operative Cases, Haubald, 1910; Medicine, 8th edition, Osler, 1912; Obstetrics, Williams; Internal Diseases, Forchheimer 1 vol., 1907; Diagnosis and Treatment of Diseases, Caille, 1905; Internal Medicine, Butler, 1907; Infancy and Childhood, Holt, 1911; Minor Surgery, Foote, 1907; Clinical Symptomatology, Pick, Heck, Koessler, 1911; Chemical and Microscopical Diagnosis, Wood, 1909; Tuberculosis, Klebs, 1909; Vitality, Fasting and Nutrition, Carrington, 1908; 8 vols. Surgery, Bryant and Buck, 1908; 3 vols. Surgical Diagnosis, Johnson, 1909; Modern Clinical Medicine (Appeltons), 4 vols., 1906; Electricity in X-Ray and Therapeutics, Monell, no number; Nervous System, Bailey, 1906; Pathology, Stengel, 1898; Pathology Technique, Mallory and Wright, 1904; Physiology, Foster—very old book; Diseases of Women, Skene, 1897; Gynecology, Kelley, 2 vols., 1908; Forensic Medicine and Toxicology, 1895; Surgery, Park—7—1901; Midwifery, Playfair; Medicine, Osler, 1898; Fractures, Beck; Anatomy, Cunningham, 1905; Hygiene, Rohe; Dermatology, Pusey, 1907; 2 vols. Medicine, Dieulafoy, no date; 4 vols. Internal Diseases, 1914, Billings; *Materia Medica*, Potter, 1890; Fractures, Scudder, 1901; Obstetrics, King, 1886; Modern Surgery, Aeosta, 1898.

**Edema and Nephritis.** Martin H. Fischer, 1915. John Wiley & Sons, New York.

Fischer is convinced that the living body tissues react to changes in their environment in a manner which is analogous to the behavior of colloids such as fibrin and gelatine. His book is a presentation of this thesis, and the phenomena of edema and nephritis are discussed and explained on the basis of this hypothesis.

The book is cleverly written and would be convincing if all disturbing physiological and pathological facts could be eliminated from the reader's memory. It is stimulating, but probably not in the direction intended. The average reader will not be inclined to follow Fischer's advice to test the validity of his hypothesis by experiments on patients, but he will be stimulated to examine into the basis of his argument. In so far as the book succeeds in accomplishing this, it will have done a service to medicine, for there can be no doubt that colloid phenomena are very important factors in the cell metabolism, factors which have been necessarily neglected in the past because of our want of knowledge of these processes even as they occur outside of the body.

A cursory review of the known facts in colloid chemistry will convince anyone that they lack the simplicity which is apparent in Fischer's presentation of them. It will be found that there are very wide differences in the behavior of the same colloid under the same experimental conditions, and that the greatest difficulty is found in obtaining concordant results. This arises from the instability of colloidal solutions, and makes it very unsafe to generalize. Young (Infection and Resistance. Zinsser 1914) closes a short review of the relation of colloidal phenomena to biological processes with the following remarks: "What is now greatly needed is more data on a greater

variety of colloids than have heretofore been investigated and work directed toward the preparation of colloidal solutions of definite character. Until something has been accomplished in these directions all biological analogies and the like cannot be anything more than qualitative, and the same holds true for many of the physical and chemical conclusions which have been discussed in this chapter."

Fischer in his discussion of theories other than his own shows a great capacity for trenchant criticism, and it is therefore to be regretted that he does not apply the same critical faculty in the interpretation of his own results. A glance through recent literature will show that those who are engaged in experiments similar to those he details are much more conservative than he is in drawing analogies. The following conclusions are taken from three recent papers. It is to be noted that these workers are fully in sympathy with Fischer's endeavor to apply the facts of colloid chemistry in the interpretation of biological processes.

Ehrenberg (Arch. f. die ges. Physiol., 1913, 153, 1), concludes that when living muscle tissue is immersed in various salt solutions, the changes can be explained on osmotic but not on colloidal principles. It is only when the tissue dies that it behaves like a colloid. Kidney tissue changes under the same conditions cannot be explained fully either on a purely osmotic or on a purely colloidal hypothesis. It is necessary to assume a "Tätigkeit" in regard to the mechanism of which we as yet know nothing.

Siebeck (Arch. f. die ges. Physiol., 1912, 148, 443), finds that qualitatively living kidney tissue in various salt solutions acts as does an osmotic cell, but the changes are not quantitatively the same, for the changes produced are only about one-fourth the magnitude of those occurring in an osmotic cell. He finds that changes in reaction have no effect on the kidney while it is alive, but when it is dead the tissue alters in weight in acid and alkaline solutions independently of the osmotic pressure. Finally, he concludes that no analogy is possible between colloid phenomena and the behavior of living kidney tissue, and he cites experiments which directly controvert those of Fischer's.

Hess and Müller (Zeit. f. exper. Path. u. Ther., 1914, 17, 59), say: "Wenn Martin Fischer's geistvoller Versuch, die ganze Oedemfrage von einer ähnlichen Gesichtspunkte aus schematisch zu lösen, als gescheitert angesehen werden wird, so weisen doch seine und Reichardt's Untersuchungen einen neuen Weg, der gangbar und hoffnungsvoll erscheint."

It is noteworthy that the first two authors definitely conclude that the reactions of dead tissue are qualitatively as well as quantitatively different from those of living tissue. This goes to the root of the whole question, and stands in direct opposition to Fischer's method of arguing from the behavior of gelatine plates and solutions of powdered fibrin, that similar changes occur in the body. Fischer rather contemptuously rejects the possibility of there being any such qualitative difference, without however giving any satisfactory reason.

So much for the theoretical basis of the book. The practical application to the problems of edema and nephritis is very interesting and full of statements which call for criticism, but in order to make this review of reasonable length we shall confine ourselves to Fischer's discussion of nephritis.

Nephritis, he says, is caused by "the abnormal production or accumulation of acid and of substances which in their action upon colloids behave like acid, in the cells of the kidney."

The first evidence he brings forward in support of this statement is the supposed fact that the urine is abnormally acid in nephritis. He

quotes a few estimations of Höber as his authority for this, and refers vaguely to "the scores" (of acidity estimations) "that may be found in any of the larger monographs on nephritis." But as a matter of fact there are no reliable data on the acidity of the urine in nephritis. It must be remembered that it would be just as inaccurate to draw conclusions from the acidity of the urine unless the dietary conditions were known, as it would be to attempt to judge the rate of protein metabolism without knowing the amount of nitrogenous food taken. It is not by any means certain that the urine is unusually acid in nephritis. The reviewer has at present under observation two cases of glomerular nephritis, who excrete a urine neutral to litmus, when on a diet which gives rise to an acid urine with normal people. And this is what might reasonably be expected in any severe kidney lesion, since the secretion of an acid urine from neutral blood is due to work on the part of the kidney, which it may not be able to accomplish when diseased.

Fischer makes a good deal of the value of changes in the acidity of the urine as a guide to diagnosis and prognosis in nephritis. So it is all the more remarkable that in the twenty clinical cases of nephritis presented that the acidity of the urine is mentioned in only four and then in the most perfunctory manner and with no details as to the diet, or even as to whether the specimen examined was from a 24-hours' collection or not. The urine is said to be "acid," "intensely acid," or "acid to paranitrophenol" before treatment by alkalis, while one case is detailed in whom the urine was acid to methylorange after sodium carbonate had been injected intravenously.

A second point brought forward to support the conception of nephritis as due to increased acidity is the high absolute and relative amount of ammonia in the urine. He states that in generalized nephritis the ammonia will amount to 2, 3, or even 4 grams a day (p. 643). This statement is interesting because it is at complete variance with the facts as given by others, and it is unfortunate that no details of the cases and no other facts of any description are given. Until such details are forthcoming we must continue to believe that in nephritis there is no increase in ammonia excretion.

Von Noorden in *Metabolism and Practical Medicine*, vol. II, p. 449, in reviewing the literature on this point says: "The subjects of renal disease excrete small quantities of ammonia" (on a diet poor in protein) "and on a varied dietary normal quantities of ammonia." "This is equally true of all forms of nephritis."

The third point is that all these conditions which are known to produce nephritis or at least albuminuria, such as interference with the circulation of the kidney, uranium, lead, etc., do so because they lead to the production of acid in the kidney or in the body. This seems, however, to be a mere assumption. If an albuminuria is produced by clamping the renal artery, it would seem rather begging the question to suppose that the acids, if any, produced under these conditions are the direct cause. There are many other possible disturbances in cell metabolism which might be responsible.

Fischer then deals with the question of albuminuria and comes to the conclusion that the albumen in the urine is derived from the solution of the kidney tissue protein, apparently mainly because fibrin will dissolve in acid solutions. It may be stated in passing that it must be obvious to Fischer that the concentration of H ions used in these experiments is enormously greater than any which can exist in the body fluids. But this does not deter him from drawing an analogy between fibrin solution in hydrochloric acid and albuminuria in nephritis, and then tacitly arguing back and implying that because of the fact that

there is an albuminuria, there must be an acidosis in the kidney. He then closes the argument by a discussion of the morphological changes in nephritis, which he considers may be reproduced by the action of acids on kidney tissue.

In the next section he takes up the "alleged consequences of kidney disease," and there is much that is sensible and to the point in his discussion of the relation of vascular disease to nephritis, but here again he shows a want of balance, and a tendency to neglect to mention facts which do not fit into his scheme. He states, for instance, very dogmatically that reduction in the amount of kidney tissue does not induce cardiac hypertrophy, and he shows photographs of animals who have had all but  $\frac{1}{4}$  to  $\frac{1}{8}$  of their kidney tissue removed. But how are we to tell whether their hearts are hypertrophied or not? Certainly not from the photographs. Has Fischer never heard of the analogous experiments of Heinike and Passler, who produced cardiac hypertrophy in this way?

Uremia is very simply explained by Fischer. It seems perfectly obvious to him that it is only an edema of the central nervous system produced by the swelling of the colloids under the influence of acids. It has nothing to do directly with nephritis. In the uremia of so-called chronic interstitial nephritis there is no kidney insufficiency. It is due to acidosis of the brain from insufficient oxygen supply because of vascular disease. The defective elimination of phenol sulphurphthalein in this type of uremia is easily passed by with the remark that this requires to be "restudied." The accumulation of non-protein nitrogen in the blood does not seem to be sufficiently important for mention.

There is a short historical review of theories of kidney secretion. Even at the risk of seeming hypercritical, it is worth while to remark that it is not justifiable to couple Bowman's name with Ludwig's as jointly responsible for the filtration theory. This is not a serious error because it is so obvious, but close to it on p. 507 and p. 508 is a more subtle but dangerous mistake, since it amounts to a misrepresentation of some very important work.

Fischer says: "To render secretion possible we must first of all supply the kidney with oxygen. In the process of water secretion by the kidney the oxygen is not only used up but carbonic acid is produced, and the loss of one and the production of the other run the higher, the greater the amount of water secreted by the kidney." He refers to the work of Barcroft and Brodie in making this statement. The impression left on the mind is that the secretion of water is accomplished by means of work on the part of the kidney, and this implication supports Fischer's theory of the primary importance of water excretion, the excretion of solid substances being nearly secondary. On this, in part, he bases his preference of the diuresis following the administration of water as a test of kidney function, and his statement that no insufficiency of function is possible while water excretion is intact (p. 628).

But if the two papers he refers to are consulted it will be found that Barcroft and Brodie find that, though diuresis is accompanied by an increase in oxygen consumption, there is no direct proportion between the oxygen used up and the amount of urine excreted, and in the second paper that the diuresis produced by urea and sodium sulphate is accompanied by a great increase in oxygen consumption.

Fischer's presentation of the essence of this work is not justified by the papers he quotes and is in direct contradiction to the further development of research along these lines. Later it was shown very clearly that it was possible to obtain a great increase in water excretion by the kidney by sodium chloride injections, without any increased

consumption of oxygen, whereas a much smaller increase of urine caused by urea or sodium sulphate produced a great increase in the amount of oxygen used. The excretion of a watery urine isotonic with the blood is not associated with evidences of chemical work.

It is very much to be hoped that in future editions this false impression of the results of Barcroft's work be corrected, since they form, as Fischer himself says, one of the "few experimentally well-established facts" on this subject. In Section IX Fischer enters on the "experimental foundations for the treatment of nephritis." These consist of experiments which are believed to show that the injection of hypertonic sodium chloride solution, or mixtures of various salts in greater concentration than they occur in the blood, is beneficial in nephritis. He shows that the albuminuria and cylinduria which appears when rabbits are tied "snugly" into a holder, or when acid is injected into the blood, or when the renal vessels are temporarily closed, disappears or diminishes when salt solution is injected.

But this "foundation" does not seem to be very firm. By means of the hypertonic salt solution a very pronounced diuresis is produced, and the volume of the urine increases to more than ten times its previous level. Of course the intensity of qualitative albumen tests diminishes and casts become difficult to find. It may be further noted that in the so-called "asphyxial nephritis" produced by tying rabbits on to a holder, all the controls recovered, while of the four injected with salt one died, and that both the animals, into whom salt as well as acid were injected, died. This does not seem a very good foundation for a proposed method of treatment.

In the following section he proceeds to the treatment of nephritis. As regards diet he says: "Practically expressed, I let the nephritic eat pretty much as he pleases." He gives enough alkali to keep the urine neutral to litmus, plenty of salt, and plenty of water. In severe cases he advises the intravenous injection of a solution of sodium carbonate and sodium chloride.

It is to be hoped that no clinician will be so carried away by the brilliancy of Fischer's arguments that he will apply his methods to the usual cases of nephritis he meets in his practice. He should remember that Fischer does not believe that a patient with uremia arising during the course of a chronic kidney disease associated with high blood pressure is suffering primarily from kidney insufficiency. Apparently in such cases he does not recommend intravenous alkaline injections, for there is no such case mentioned among his clinical cases, although it is difficult to understand why not, for he says that uremia also is due to acid accumulation.

The best advice that can be given anyone who feels tempted to try Fischer's treatment is to read carefully and critically the case reports he cites. He will find two cases of post-operative anuria, three cases of apparently acute nephritis, two cases diagnosed as chronic parenchymatous nephritis, one obscure case (No. 26) in which no diagnosis seems possible from the facts given, and ten cases of albuminuria and cylinduria associated with pregnancy. One other case diagnosed as one of the "acute nephritis" in which death followed an intravenous injection of hypertonic salt solution and sodium carbonate, is given. A post-mortem examination was obtained and the following description of the condition found in the kidneys is characteristic of the character of these reports: "The kidneys were somewhat swollen and of good color. The capsules stripped easily!"

It is surely within the bounds of moderation to say that such vague and slipshod summaries as are presented here are far from convincing. The mere fact that a diuresis may be induced in some patients who have albumen and casts in their urine by in-

travenous injection of hypertonic salt solutions, is no proof that they were necessarily benefited thereby. Nor is the decrease in the intensity of albumen reactions and in the number of casts remarkable when the urine becomes very dilute. The subsequent recovery which occurred is frequently seen without any such treatment. It is possible he is right that in an acute nephritis such treatment is beneficial; but the better way to settle the question would surely be to produce an acute experimental nephritis in animals by uranium, for instance, which he specifically mentions as acting by leading to an acid accumulation in the kidneys, and to try the effect of his injections on them. He could then bring forward objective proof of the presence of an acute kidney lesion, and leave no doubt in his reader's mind as to the accuracy of his diagnosis, a doubt which certainly remains after reading his clinical reports.

If this book were not clever and interesting, if it did not contain many sound and true remarks, it would not be worth reviewing. It is because it is presented in such a forcible and compelling manner that it requires close criticism. It has all the charm of the new and unorthodox, but the new is not always true, and facts, however old, are still facts.

THOMAS ADDIS.

#### DEPARTMENT OF PHARMACY AND CHEMISTRY.

Edited by FRED I. LACKENBACH.

Since publication of New and Nonofficial Remedies, 1915, and in addition to those previously reported, the following articles have been accepted by the Council on Pharmacy and Chemistry of the American Medical Association for inclusion with "New and Nonofficial Remedies":

Standard Radium Solution for Bathing.—A 5.2 per cent. barium chloride solution containing radium chloride equivalent to 4.2 micrograms of radium per bottle. For "Actions and Uses" see the article on radium in New and Nonofficial Remedies. The barium in the solution is said to have no effect. The contents of a bottle, containing 4.2 microcuries or 10,000 Mache units are used for a bath. The Radium Chemical Co., Pittsburgh, Pa. (Jour. A. M. A., April 17, 1915, p. 1325).

Standard Radium Solution for Drinking.—A solution of 2 micrograms of radium and 1.3 mg. barium chloride per bottle of 60 c.c. For "Actions and Uses" see the article on radium in New and Nonofficial Remedies. In view of the small barium content, it is claimed that the physiologic action of barium may be ignored. The Radium Chemical Co., Pittsburgh, Pa. (Jour. A. M. A., April 17, 1915, p. 1325).

Standard Radium Earth.—A mixture consisting chiefly of silica and small quantities of carnotite, 450 gm. containing 0.45 micrograms of radium in the form of radium sulphate. For "Actions and Uses" see the article on radium in New and Nonofficial Remedies. For use the earth is mixed with water and heated for a time. The Radium Chemical Co., Pittsburgh, Pa. (Jour. A. M. A., April 17, 1915, p. 1325).

Standard Radium Compress.—A compress containing 225 gm. of a mixture consisting chiefly of silica and barium sulphate containing radium sulphate equivalent to 15 micrograms of radium. For "Actions and Uses" see the article in New